REMARKS

Claim 34 has been amended as set forth above. Exemplary support for the amendment to Claim 34 is found at page 80, lines 23-29. Thus, no new matter is added by the amendment of Claim 34.

Applicants respond below to the remaining rejections raised by the PTO in the final Office Action mailed March 28, 2005. For the reasons set forth below, Applicants respectfully traverse.

Correction of Inventorship under 37 CFR §1.48(b)

Applicants request that several inventors be deleted, as these inventors' inventions are no longer being claimed in the present application as a result of prosecution. The fee as set forth in § 1.17(i) is submitted herewith.

Information Disclosure Statement

The Examiner asserts that the previously filed information disclosure statement fails to comply with 37 C.F.R. § 1.98(a)(2). The Examiner asserts that the Blast results are not true publications with a publication date, and therefore, are not fully in compliance with 37 C.F.R. § 1.97.

Applicants submit herewith an Information Disclosure Statement with additional information on the BLAST results, including the publication dates of the cited sequences.

Rejections under 35 U.S.C. §112, first paragraph – Written Description/New Matter

The Examiner rejects Claims 22-27, 30 and 33-34 under 35 U.S.C. §112, first paragraph as lacking an adequate written description. First, the Examiner argues that "[n]o proper basis nor conception in context with that contemplated within the instant specification at the time of filing the instant application exists for now defining the extracellular domain as 'amino acids 77-310.'" The Examiner argues that Figure 20 merely discloses a transmembrane domain at amino acids 58-76, but does not specify which portion of the PRO4405 polypeptide may be extracellular. Therefore, the Examiner argues that the amendment defining the extracellular domain as amino acids 77-310 constitutes new matter.

Applicants respectfully disagree and assert that support for the recitation of the specific amino acids of the extracellular domain is found in the application as filed. Figure 20 shows the sequence of SEQ ID NO:45, and also specifies that the transmembrane domain is at amino acids 58-76. Furthermore, the specific sequence of the extracellular domain is disclosed because the specification at page 28, lines 29-32, recites that the transmembrane domain may be a type II transmembrane domain. Proteins with type II transmembrane domains have a C-terminal extracellular domain (the N-terminus is exposed to the cytoplasm). In the instant case, the transmembrane domain is disclosed as being at amino acid 58 to position 76. Thus, because PRO4405 has a type II transmembrane domain, the extracellular domain is C-terminal, that is, at amino acids 77-310. Therefore, the claim amendments defining the extracellular domain as amino acids 77-310 are fully supported by the specification as filed and do not constitute new matter.

Reconsideration and withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. §112, first paragraph – Written Description

The Examiner continues to reject Claims 22-27, 30-31 and 33-34 under 35 U.S.C. §112, first paragraph as lacking written description for the reasons previously of record and for the following additional reasons. The Examiner argues that the specification only discloses a single *human* polypeptide sequence. Based upon that, the Examiner argues that no written description is provided for sequences from species *other than humans*.

The Legal Standard for Written Description

The well-established test for sufficiency of support under the written description requirement of 35 U.S.C. §112 , first paragraph is whether the disclosure "reasonably conveys to artisan that the inventor had possession at that time of the later claimed subject matter." *In re Kaslow*, 707 F.2d 1366, 1375, 2121 USPQ 1089, 1096 (Fed. Cir. 1983); *see also Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at1563, 19 USPQ2d at 1116 (Fed. Cir. 1991). The adequacy of written description support is a factual issue and is to be determined on a case-by-case basis. *See e.g., Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116 (Fed. Cir. 1991). The factual determination in a written description analysis depends on the nature of the invention and the

amount of knowledge imparted to those skilled in the art by the disclosure. *Union Oil v. Atlantic Richfield Co.*, 208 F.3d 989, 996 (Fed. Cir. 2000).

The Current Claims Are Adequately Described

As noted above, whether the Applicants were in possession of the invention as of the effective filing date of an application is a factual determination, reached by the consideration of a number of factors, including the level of knowledge and skill in the art, and the teaching provided by the specification. The inventor is not required to describe every single detail of his/her invention. An applicant's disclosure obligation varies according to the art to which the invention pertains. The present invention pertains to the field of recombinant DNA/protein technology. It is well-established that the level of skill in this field is very high since a representative person of skill is generally a Ph.D. scientist with several years of experience. Accordingly, the teaching imparted in the specification must be evaluated through the eyes of a highly skilled artisan as of the date the invention was made.

As amended, the rejected claims are related to isolated polypeptide variants having from at least 80%, 90%, 95% or 99% amino acid sequence identity to several polypeptides related to SEQ ID NO:45. The polypeptide variants must also satisfy the limitation "wherein said isolated polypeptide has the ability to induce chondrocyte redifferentiation." In view of this, Applicants maintain that the variant claims recite sufficient distinguishing characteristics for the claimed genus of polypeptides, including polypeptides from species other than humans. Based upon the detailed description of the cloning and expression of variants of PRO4405 in the specification, the description of the assay in Example 36, the actual reduction to practice of sequences SEQ ID NOs: 44 and 45, and the functional recitation in the instant claims, Applicants submit that one of skill in the art would know that Applicants possessed the invention as claimed in the instant claims.

Applicants note that the pending claims are analogous to the claims discussed in Example 14 of the written description training materials. For reasons similar to those expressed in Example 14 of the training materials, the written description requirement should be deemed satisfied for the instant claims. A copy of Example 14 from the training materials is included herewith as Exhibit 1 for the convenience of the Examiner. In Example 14, the written description requirement was found to be satisfied for claims relating to polypeptides having a

percentage of homology (95%) to a particular sequence and possessing a particular catalytic activity. The claims were considered fully described even though the applicant had not made any variants and even though only a single representative species was disclosed. Example 14 notes that the procedures for making variants were conventional in the art and that an assay was described in the specification which will identify other proteins having the claimed catalytic activity.

Similarly, in the instant case the pending claims recite a genus of proteins without substantial variation, since the claims require a percentage of sequence identity to the disclosed sequence of SEQ ID NO:45, and require that the variant sequences have a specific functional activity, namely, the ability to induce chondrocyte redifferentiation. Also, the specification describes how to make the claimed percentage variants of SEQ ID NO:45. In addition, the specification discloses how to test to determine if a polypeptide has the ability to induce chondrocyte redifferentiation. Thus, like Example 14, one of skill in the art would conclude that Applicants "were in possession of the necessary common attributes possessed by members of the genus." Therefore, Applicants assert that the written description requirement of § 112 is satisfied for all of the pending claims.

The Examiner argues that the claimed subject matter is not described and states that the situation is analogous to the situation in *Fiers v. Revel.* 984 F.2d 1164 (Fed. Cir. 1993). The Examiner quotes from that case stating, "an adequate written description of a DNA [product] requires more than a mere statement that it is part of the invention and a reference to a potential method for isolating it; what is required is a description of the DNA itself." Furthermore, the Examiner cites to *Fiddes v. Baird* (30 U.S.P.Q.2d 1481, 1483 (Bd. Pat. App. & Int. 1993)), noting that "claims directed to mammalian FGFs were found unpatentable due to lack of written description for the broad class, in which the specification had provided an adequate written description of only the bovine sequence." Finally, the Examiner quotes from *Regents of the Univ. of Cal. v. Ely Lilly and Co.* (119 F.3d 1559 (Fed. Cir. 1997)), "[a] definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is."

Respectfully, Applicants disagree with the Examiner regarding the cited cases and assert that the instant case is very different and distinguishable from the cited cases. None of the cited

cases is closely analogous to the instant case, and particularly not as analogous as Example 14 of the training materials for PTO Examiners. For example, none of the disputed cases sought to claim sequences based upon identity or homology to a disclosed sequence in combination with a functional limitation.

Friers is distinguishable. *Friers*, involved a three way interference proceeding. *See Friers* at 1166. The claim count at issue recited "[a] DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide." *Id.* Revel was found to not have satisfied the written description requirement because he only disclosed a method for isolating a fragment of the DNA coding for beta interferon and an mRNA coding for beta interferon, but he did not disclose a complete beta interferon DNA sequence. *See id.* at 1170-71. The court argued that an adequate written description of a DNA requires more than a mere statement that it is part of the invention and a reference to a potential method for isolating it; what is required is a description of the DNA itself. Here, Applicants disclosed more than a method for isolating the variants polypeptides, and in fact, disclose a specific description of the amino acid sequence of the variants. Thus, Revel did not disclose as much identifying information as in the instant case.

Fiddes v. Baird is also distinguishable. *Fiddes* involved an interference proceeding. *See* 30 U.S.P.Q.2d at 1481. Baird sought to claim a DNA sequence encoding a mammalian FGF. *See id.* at 1482. Baird's claims did not include any structural requirements such as a requirement for a percentage of identity. The board found that Baird was not entitled to the benefit of his priority application because the written description requirement was not satisfied. *See id.* at 1484.

Likewise, *Lilly* can be distinguished. There the court stated that "a generic statement [in the claims] such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function." *See Lilly* at 1568. In contrast, the instant claims include a function and a specific structure.

Thus, the cases relied upon by the Examiner are distinguishable from the instant situation. Therefore, for the reasons set forth above, Applicants assert that one of ordinary skill in the art would recognize that Applicants possessed the claimed subject matter at the time of filing the

instant application. Hence, Applicants respectfully request that the PTO reconsider and withdraw the written description rejection under 35 U.S.C. §112.

Conclusion

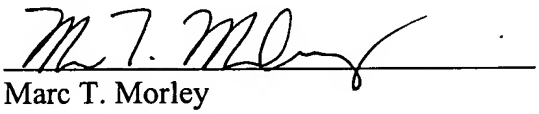
The present application is believed to be in condition for allowance, and an early action to that effect is respectfully solicited. Applicants invite the Examiner to call the undersigned if any issues may be resolved through a telephonic conversation.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: June 23, 2005

By: 

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Example 14: Product by Function

Specification: The specification exemplifies a protein isolated from liver that catalyzes the reaction of **A** $\longrightarrow$ **B.** The isolated protein was sequenced and was determined to have the sequence as set forth in SEQ ID NO: 3. The specification also contemplates but does not exemplify variants of the protein wherein the variant can have any or all of the following: substitutions, deletions, insertions and additions. The specification indicates that procedures for making proteins with substitutions, deletions, insertions and additions is routine in the art and provides an assay for detecting the catalytic activity of the protein.

Claim:

A protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A $\longrightarrow$ B.

Analysis:

A review of the full content of the specification indicates that a protein having SEQ ID NO: 3 or variants having 95% identity to SEQ ID NO: 3 and having catalytic activity are essential to the operation of the claimed invention. The procedures for making variants of SEQ ID NO: 3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO: 3 which have 95% identity to SEQ ID NO: 3 and retain its activity are conventional in the art.

A review of the claim indicates that variants of SEQ ID NO: 3 include but are not limited to those variants of SEQ ID NO: 3 with substitutions, deletions, insertions and additions; but all variants must possess the specified catalytic activity and must have at least 95% identity to the SEQ ID NO: 3. Additionally, the claim is drawn to a protein which **comprises** SEQ ID NO: 3 or a variant thereof that has 95% identity to SEQ ID NO: 3. In other words, the protein claimed may be larger than SEQ ID NO: 3 or its variant with 95% identity to SEQ ID NO: 3. It should be noted that "having" is open language, equivalent to "comprising".

The claim has two different generic embodiments, the first being a protein which comprises SEQ ID NO: 3 and the second being variants of SEQ ID NO: 3. There is a single species disclosed, that species being SEQ ID NO: 3.

A search of the prior art indicates that SEQ ID NO: 3 is novel and unobvious.

There is actual reduction to practice of the single disclosed species. The specification indicates that the genus of proteins that must be variants of SEQ ID NO: 3 does not have substantial variation since all of the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO: 3. The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity. One of skill in the art would conclude that

applicant was in possession of the necessary common attributes possessed by the members of the genus.

Conclusion: The disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention.